

AMENDED CLAIMS

1. A method of isolating fully thioated single stranded antisense oligonucleotides from a biological solution, which method comprises the steps of contacting the biological solution with an immobilised metal ion adsorption chromatography (IMAC) resin to adsorb antisense oligonucleotides to said resin and subsequently contacting the resin with an eluent under conditions that provide desorption of the antisense oligonucleotides from said resin, wherein the fully thioated antisense oligonucleotides are separated from incorrectly thioated antisense oligonucleotides in said solution.
2. A method according to claim 1, wherein the biological solution results from a synthesis of antisense oligonucleotides.
3. A method according to claim 1 or 2, wherein fully thioated antisense oligonucleotides are separated from incorrectly synthesised oligonucleotides.
4. A method according to any one of the preceding claims, wherein fully thioated antisense oligonucleotides are separated from incorrectly thioated antisense oligonucleotides containing 1-5, such as 1 or 2, bonds without thioation.
5. A method according to any one of the preceding claims, wherein the metal ion is  $Zr^{2+}$  or  $Fe^{3+}$ .
6. A method according to any one of the preceding claims, wherein the antisense oligonucleotides are of a size in the range of 5-30, and preferably 15-25, base pairs.
7. A method according to any one of the preceding claims, wherein the pH of the biological solution is below about 7 during the adsorption of antisense oligonucleotides.
8. A method according to any one of the preceding claims, which in addition comprises a subsequent step of polishing the isolated antisense oligonucleotides.
9. Use of an immobilised metal ion adsorption chromatography (IMAC) resin for isolation of fully thioated single stranded antisense oligonucleotides from incorrectly thioated antisense oligonucleotides in a biological solution.